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| 10/026,914 | 12/27/2001 | Birgit Linhart | 0273-0006 | 6890 |

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Shanks & Herbert
TransPotomac Plaza
Suite 306
1033 N. Fairfax
Alexandria, VA 22314

| EXAMINER | |
|---|---|
| HINES, JANA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/026,914 | LINHART ET AL.5 | |
| | Examiner | Art Unit | |
| | Ja-Na Hines | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,9,13-15 and 20-26* is/are pending in the application.

4a) Of the above claim(s) *7 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 13-15, 20-21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Amendment Entry*

1. The amendment filed February23, 2004 has been entered. Claims 1-6, 13-15, and 20 have been currently amended. Claim 26 has been newly added. Claims 8, 10-12, 16-19 have been cancelled. Claims 7-12, 22-25 have been withdrawn. Claims 1-6, 13-15, 20-21 and 26 are under consideration in this office action.

### *Withdrawal of objections and Rejections*

2. The following objections and rejection have been withdrawn in view of applicants' amendments and arguments:

a) The objection of claims 20 and 21;

b) The rejection of claims 4-5 under 35 U.S.C. 112, second paragraph; and

c) The rejection of claims 1, 4-6,13-15 and 20-21 under 35 U.S.C. 102(b) as being anticipated by King (US Patent 5,804,201).

### *Response to Arguments*

3. Applicant's arguments filed February 23,2 004 have been fully considered but they are not persuasive.

4. The rejection of claims 13-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The rejection was on the grounds that the specification and claims lack sufficient written description of the polynucleotide encoding the hybrid polypeptide. There is no description of the nucleic

acids that must encode the hybrid polypeptide. The instant specification does not provide for the structure of the polynucleotide. The specification does not provide a teaching of the entire structure, showing that nucleic acids were isolated at the time the invention was made.

Applicants assert that an inventor need not explain every detail since he is speaking to those skilled in the art, and therefore the instant claims point out and distinctly described the claimed method. However, an essential element of the claims is a polynucleotide that has a full-length open reading frame which is essential to the operation /function of the invention as described in the specification. In principle, the same sequence can be translated in any one of the reading frames, each of which will specify a completely different polypeptide chain. Applicants have not taught a sufficient description of a genus of the polypeptide encoded by a polynucleotide. There is no conception of the genus of polypeptides as claimed at the time of filing. Furthermore, applicants have not taught what the polynucleotide is that encodes the polypeptide. The specification does not teach the open reading frames for any polynucleotide. Applicant does not know what is encoded by the polynucleotide, in view of the lack of teaching. In view of the plethora of possible reading frames, there is no teaching what encoded polypeptide would be. There is no teaching of a representative polynucleotide encoding a polypeptide. Thus, there is no conception of the genus of polynucleotides encoding polypeptides when no polypeptides are taught by the specification. In view of applicants' failure to explain the essential details like a polynucleotide sequence that encodes the claimed polypeptide, the rejection is maintained.

Applicants assert that the generic steps for providing a polynucleotide that encodes a polypeptide are known in the art, therefore applicants have particularly and distinctly pointed out the claimed methods. However, the specification does not provide functional or structural characterization of the full-length open reading frame of the instantly claimed polynucleotide. The specification does not provide a clear protocol by which the polynucleotide at the time the invention was made. The specification does not provide structural characterization of the complete open reading frame of the antigen, i.e., including a start and stop codon. In the instant case, the classic start codon, methionine, is missing from the beginning of the cloned nucleic acid from which the sequence of the polynucleotides were derived. The specification does not provide evidence that any polynucleotide, as claimed, functions with the ability to encode the hybrid polypeptide. In view of the lack of guidance, it is apparent that Applicants were not in possession of polynucleotides that encoded the hybrid polypeptide, at the time of filing the instant application. The skilled artisan cannot envision the detailed structure of the polynucleotide, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation, contrary to applicants arguments. Encoding distinguishes the claimed polynucleotides from unclaimed sequences only by what they do, which is a purely functional distinction, it does not disclose a structure. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant specification fails to describe a polynucleotide since function of the polynucleotide does not describe the claimed polynucleotide itself.

Courts have found that the claimed polynucleotide, which fails to disclose a representative sequence, described only by its ability to encode, may describe its function, but it does not describe the polynucleotide itself. A description of genetic material by what it does - such as encoding - is insufficient to satisfy 35 U.S.C. 112, first paragraph. *In re Deuel*, 51 F.3d 1552, 1558-59, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995). Moreover, a disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein. The existence of a general method of gene cloning in the prior art is not sufficient, without more, to render obvious a particular cDNA molecule. Additionally, it is noted that applicants failed to point to a representative polynucleotide that has the ability to encode the claimed polypeptide. Thus, in the absence of sequence information as claimed herein a polynucleotide described only by its ability to encode a polypeptide fails to meet the requirements of 35 U.S.C. 112, first paragraph and applicants arguments are not persuasive.

5. The rejection of claims 1-3 and 13-14 under 35 U.S.C. 102(b) as being anticipated by Vrtala et al., (1996. J. Allergy Clin. Immun. Vol. 97(3): 781-787) is maintained for reasons already of record. The rejection was on the grounds that Vrtala et al., teach a hybrid polypeptide comprising at least two different allergenic proteins, specifically the timothy grass pollen allergens Phl p1 and Phl p 2. These are the complete allergenic proteins as the cDNA used for encoding the mature protein.

Therefore, Vrtala et al., teach a polynucleotide with encodes a polypeptide that meets the claimed limitations. Vrtala et al., also teach a method for preparing a hybrid polypeptide using PCR technology comprising the same steps as recited by the instant claims.

Applicants assert that Vrtala et al., do not teach the claimed polypeptide because Vrtala et al., demonstrate that the allergens can be converted into hypoallergenic fragments. In response to applicant's argument that Vrtala et al., demonstrate that allergen can be converted into hypoallergenic fragments, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Moreover, Vrtala et al., teach that DNA coding for three major timothy grass pollen allergens representing group I (Phl p1), group II (Phl p 2) and group V (Phl p 5) was known and the construction of the expression plasmids for Phl p 1, Phl p 2 and Phl p 5. Vrtala et al., teach Phl p 1 and Phl p 2, both of which contained ATG start codon in front of the coding region of the mature protein and genes were then inserted as fragments whereby expression of the recombinant allergens was also taught and the cells were cultured, expressed, purified and recovered. Applicants have failed to particularly point out the structural difference between the polypeptide taught by Vrtala et al., and the polypeptide instantly claimed.

Applicants urge that Vrtala et al., do not teach the claimed polypeptide because

Vrtala et al., teach a preparation of a cocktail including Phl p1, Phl p2, and Phl p5 which were transcribed by PCR. However, despite Vrtala et al., intention or use of the polypeptide, Vrtala et al., taught a hybrid polypeptide comprising at least two different allergenic proteins or fragments wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein.

Applicants note that Vrtala et al., do not show any experiments describing the generation of hybrid vaccines, however the claims are not drawn to hybrid vaccines. Therefore a recitation of the intended use, such as a hybrid vaccine, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Moreover, the lack of experimentation is not relevant to the instant claimed polypeptides since applicants have failed to point to structural differences.

Additionally applicants' refer to the hybrid polypeptides inducing vigorous anti-Phl p1, anti-Phl p2, and anti-Phl p6 antibody response in comparison to individual allergens and the induction of stronger antibody responses; however the claims are not drawn to the vigorous antibody responses or stronger antibody responses. The claims are merely drawn to hybrid polypeptide with no requirements drawn to antibody responses. Therefore, applicants arguments are not persuasive, since the instant claims fail to require such reactions.

Applicants assert that Vrtala et al., do not refer to using two or more major timothy grass pollen allergens. In response to applicant's argument that the Vrtala et al., reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., two or more major timothy grass pollen allergens are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims only require plant allergen polypeptides and Vrtala et al., teach such, therefore Vrtala et al., meet the claimed limitations.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 13-15, 20-21 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a hybrid polypeptide comprising at least two different plant allergenic proteins or fragments thereof, wherein each fragment consists of at least eight consecutive amino acids of the respective allergenic protein.

The claims drawn to the fragments thereof wherein the fragments consist of amino acid sequences that fail to recite any associated function. Furthermore, it is unclear how to define fragments thereof with respect to what amino acids must be comprised therein to acquire the appropriate fragments. Neither the claims nor the specification teach how to obtain such fragments thereof. There is no guidance as to what amino acids may or may not be included without causing a detrimental effect to the fragments thereof as claimed. The claims broadly recite fragments thereof, therefore any fragments thereof is being claimed, and no specific location requirement for particular amino acids is recited. Thus, the resulting fragments thereof could result in a functional fragment not taught and enabled by the specification. There is no written description of which eight amino acids must be comprised in the claimed hybrid polypeptide.

Moreover, without an associated function, the claims fail to limit the unidentified sequences encompassed by applicants' claims. It is noted that there is no requirement that the polypeptides have an ascertainable activity associated with the hybrid polypeptide. Furthermore any variant or mutant that has eight consecutive amino acids yet have a different function is also encompassed by the claims. Moreover, there is no requirement that the at least eight amino acids must be from a region is highly conserved region in the plant allergen. Therefore, the specification lacks adequate

support for the claims. Thus, the structure of sequences having sufficient activity have not been defined and thus broadens the scope of the invention to encompass any amino acid sequences. Furthermore, the structure of sequences having sufficient activity has been not described by the instant specification.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus, including a functional activity. With the exception of specifically recited sequences the skilled artisan cannot envision the detailed structure of the fragments thereof, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid and amino acids sequences themselves are required. See *Fiers v. Revel*, 25

USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of amino acids by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Currently the instant claims lack an adequate description of both the fragments thereof and the function of the polypeptide, thus the descriptions are insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 24, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600